DETAILED ACTION

1. Interference No. 105,208 has been terminated by granting a request of the Dietz-Band party for adverse judgment. *Ex parte* prosecution is resumed.

2. This application has been reassigned to a new examiner.

Status of the Claims

3. Claims 127-143 are pending.

Claims 127-143 are rejected.

Claims 130, 138, and 141 are objected to.

Priority

4. This application repeats a substantial portion of prior Application No. 09/765,291 filed 22 January 2001, and adds and claims additional disclosure not presented in the prior application. **Since this application names an inventor or inventors named in the prior application, it constitutes a continuation-in-part of the prior application.** Should applicant desire to obtain the benefit of the filing date of the prior application, attention is directed to 35 U.S.C. 120 and 37 CFR 1.78. **Benefit for the claimed subject matter regarding products comprising two probes that are substantially complementary to an entire breakpoint regions is not granted to any of the applications for which benefit is claimed under 35 U.S.C. 120 because the claimed subject matter is not described in the parent applications.**

5. It is noted that this application contains subject matter common to prior Application Nos. 09/765,291, 08/487,974, 08/342,028, 08/181,367, 08/054,353, 07/537,305, 07/497,098, and 07/444,669. **A reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an application data sheet (37 CFR 1.76), if**

applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a) Although the preliminary amendment to the first sentence in the transmittal paper was filed prior to adoption of the current rule regarding amendment to the specification, the applicants are requested to submit an amendment to the specification or an Application Data Sheet to perfect their claim for priority. For benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. A review of the claim for priority in the transmittal paper filed 30 June 2003 shows that many of the stated relationships are incorrect. For example, the instant application was not filed as the result of a restriction requirement in Application No. 09/765,291, and is not a divisional of that application. If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior

application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Information Disclosure Statement

6. The information disclosure statement (IDS) submitted on 18 March 2010 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure

statement is being considered by the examiner. Some copies of references were not provided and have been lined through to indicate they were not considered.

7. The Information Disclosure Statement filed 18 March 2010 does not contain a legible copy of each reference listed on the list of references. It is not known whether this is an error of the applicants or a scanning error by the Office. Consequently the missing references have been listed as not considered in the signed copy of the list of references attached to this Office action. If the applicants provide a legible copy of the missing references in response to this Office action, the references will be considered under 37 CFR 1.97(f), and a signed copy of the list of references indicating consideration of the missing references will be provided to the applicants without the necessity of the applicants filing a second Information Disclosure Statement.

Oath/Declaration

8. This application presents a claim for subject matter not originally claimed or embraced in the statement of the invention. The Declaration filed 30 June 2003 does not identify the instant application or the preliminary amendment that contains subject matter not present in the application number identified on the declaration (see MPEP 602V, 608.04(b), and 714.01(e). Applications filed prior to 21 September 2004 require acknowledgement of preliminary amendments in the declaration. A supplemental oath or declaration is required under 37 CFR 1.67. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02.

9. Regarding the appointment of associate attorney in the paper accompanying the Declaration, the Office has discontinued the practice of associate attorneys effective 25 June 2004 (see MPEP 402.02).

Drawings

10. The specification mentions drawings with features in color in the Brief Description of the Drawings on pages 26-33. No color drawings are present in the application file. Under the assumption that the drawings are intended to be color drawings, the drawings are objected to.

11. Color photographs and color drawings are not accepted unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

Claim Objections

12. Claims 130, 138, and 141 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claims are drawn to a product comprising at least one probe, but depend from a claim requiring at least two probes. Therefore claims 130, 138, and 141 are broader than the claim from which they depend.

Claim Rejections - 35 USC § 112

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 127-143 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed subject matter is a product comprising two DNA probes that are complementary to and span a breakpoint region of DNA. The probes are required to hybridize to both sides of the breakpoint region. The specification describes in figure 8 and page 116 two probes that hybridize to one side of BCR and Abl breakpoints. The BCR probe PEM12 is indicated in figure 8 to span the BCR breakpoint. The Abl probe c-hu-abl is shown to be entirely to the right of the Abl breakpoint in the map of figure 8. However the following passages in page 116 of the specification makes explicit that neither probe hybridizes to both sides of a breakpoint:

> The approximate location of the 18 kb phage PEM12 probe (the BCR probe) is indicated by the open horizontal bar. Since the majority of breakpoints in CML occur between exons 2 and 4, 15 kb or more of target for PEM12 will remain on the Philadelphia chromosome. In the classic reciprocal translocation a few kb of target for PEM12 (undetectable fluorescent signal)will be found on the derivative chromosome.
>
> Exons of the ABL gene are depicted as open vertical bars (not to scale). The Roman numerals Ia and Ib refer to the alternative first exons, and II to the second exon. Exon II is approximately 25kb upstream of the end of

the 28 kb cosmid c-hu-abl (the ABL probe). All CML breakpoints occur upstream of exon II, usually between exons Ib and Ia, within a region that is approximately 200kb in length. Thus, c-hu-abl will always be 25 to 200 kb away from the fusion junction.

The specification discusses a genus of probe on page 19 as follows:

This invention provides for nucleic acid probes that reliably stain targeted chromosomal materials in the vicinity of one or more suspected genetic rearrangements. Such nucleic acid probes useful for the detection of genetic rearrangements are typically, of high complexity. Such nucleic acid probes preferably comprise nucleic acid sequences that are substantially homologous to nucleic acid sequences in chromosomal regions that flank and/or extend partially or fully across breakpoints associated with genetic rearrangements.

This passage does not describe the claimed product of two probes because it does not require two probe that must hybridize to both sides of a breakpoint region. Instead the passage is generic to the claimed subject matter. Neither of the two examples of probes noted above meet the limitations of the claimed subject matter. Even if it was argued that the BCR probe PEM12 inherently could hybridize to both sides of a breakpoint if the breakpoint were sufficiently within the region the probe is complementary to, the specification does not describe such a possibility, and the claims require two probes that hybridize to both sides of a breakpoint region. The specification does not describe the structure of a representative number of species of the claimed genus to describe the claimed subject matter.

The CAFC recently held that 35 U.S.C. 112 first paragraph has a separate written description requirement and that generic claims must describe a representative number of species or a correlation between the claimed function and structure of the claimed product to describe a claimed genus. See Ariad Pharmaceuticals Inc., Massachusetts Institute of Technology, The Whitehead Institute for Biomedical Research, and The President and Fellows of Harvard College v. Eli Lilly and Company (United States Court of Appeals for the Federal Circuit, Case No.

2008-1248, Decided March 22, 2010, available at http://www.cafc.uscourts.gov/opinions/08-1248.pdf)

At pages 20-23:

Although many original claims will satisfy the written description requirement, certain claims may not. For example, a generic claim may define the boundaries of a vast genus of chemical compounds, and yet the question may still remain whether the specification, including original claim language, demonstrates that the applicant has invented species sufficient to support a claim to a genus. The problem is especially acute with genus claims that use functional language to define the boundaries of a claimed genus. In such a case, the functional claim may simply claim a desired result, and may do so without describing species that achieve that result. But the specification must demonstrate that the applicant has made a generic invention that achieves the claimed result and do so by showing that the applicant has invented species sufficient to support a claim to the functionally-defined genus.

Recognizing this, we held in Eli Lilly that an adequate written description of a claimed genus requires more than a generic statement of an invention's boundaries. 119 F.3d at 1568. The patent at issue in Eli Lilly claimed a broad genus of cDNAs purporting to encode many different insulin molecules, and we held that its generic claim language to "vertebrate insulin cDNA" or "mammalian insulin cDNA" failed to describe the claimed genus because it did not distinguish the genus from other materials in any way except by function, i.e., by what the genes do, and thus provided "only a definition of a useful result rather than a definition of what achieves that result." Id.

We held that a sufficient description of a genus instead requires the disclosure of either a representative number of species falling within the scope of the genus or structural features common to the members of the genus so that one of skill in the art can "visualize or recognize" the members of the genus. Id. at 1568-69. We explained that an adequate written description requires a precise definition, such as by structure, formula, chemical name, physical properties, or other properties, of species falling within the genus sufficient to distinguish the genus from other materials. Id. at 1568 (quoting Fiers v. Revel, 984 F.2d 1164, 1171 (Fed. Cir. 1993)). We have also held that functional claim language can meet the written description requirement when the art has established a correlation between structure and function. See Enzo, 323 F.3d at 964 (quoting 66 Fed. Reg. 1099 (Jan. 5, 2001)). But merely drawing a fence around the outer limits of a purported genus is not an adequate substitute for describing a variety of materials constituting the genus and showing that one has invented a genus and not just a species.

In fact, this case similarly illustrates the problem of generic claims. The claims here recite methods encompassing a genus of materials achieving a stated useful result, i.e., reducing NF-κB binding to NF-κB recognition sites in response to external influences. But the specification does not disclose a variety of species that accomplish the result. See Eli Lilly, 119 F.3d at 1568 ("The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention."). Thus, as indicated infra, that specification fails to meet the written description requirement by describing only a generic invention that it purports to claim.

We also specifically addressed and rejected Ariad's argument regarding original claims in Fiers, 984 F.2d at 1170, and again in Enzo, 323 F.3d at 968. In Fiers, we rejected the argument that "only similar language in the specification or original claim is necessary to satisfy the written description requirement." 984 F.2d at 1170 (emphasis added). Rather, we held that original claim language to "a DNA coding for interferon activity" failed to provide an adequate written description as it amounted to no more than a "wish" or "plan" for obtaining the claimed DNA rather than a description of the DNA itself. Id. at 1170-71. That Fiers applied § 112, first paragraph, during an interference is irrelevant for, as we stated above, the statute contains no basis for ignoring the description requirement outside of this context. And again in Enzo we held that generic claim language appearing in ipsis verbis in the original specification does not satisfy the written description requirement if it fails to support the scope of the genus claimed. 323 F.3d at 968. We concluded that "[a] claim does not become more descriptive by its repetition, or its longevity." Id. at 969.

Ariad argues that Eli Lilly constituted a change in the law, imposing new requirements on biotechnology inventions. We disagree. Applying the written description requirement outside of the priority context in our 1997 Eli Lilly decision merely faithfully applied the statute, consistent with Supreme Court precedent and our case law dating back at least to our predecessor court's Ruschig decision. Neither the statute nor legal precedent limits the written

description requirement to cases of priority or distinguishes between original and amended claims. The application of the written description requirement to original language was raised in Fiers, Eli Lilly, and Enzo, and is raised again by the parties here. Once again we reject Ariad's argument and hold that generic language in the application as filed does not automatically satisfy the written description requirement.

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claims 127-143 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 127-143 are indefinite for recitation of the phrase "an entire breakpoint region" because it is not clear if the breakpoint region is a region of DNA prior to or after a genomic translocation. The phrase is further indefinite because it is not clear how "an entire" affects the metes and bounds of the breakpoint region. The rejection would be overcome by amendment the claims to recite "a breakpoint region prior to translocation" as supported at least in Figure 8.

For the purpose of examination, the claims have been assumed to incorporate the suggested amendments.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 127-143 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dewald et al. (Blood Vol. 91, pages 3357-3365 (1998)).

The claimed subject matter is a product comprising two DNA probes that are complementary to and span a breakpoint region of DNA. The probes are required to hybridize to both sides of the breakpoint region. In some embodiments the probes are in containers or a kit comprises the probes. In some embodiments the probes are detectably labeled. In some embodiments the probes are for the Abl and BCR breakpoints.

Dewald et al. shows a process of using two probes that span the breakpoints of the Abl and BCR genes in the abstract and throughout. In the first column of page 3357 Dewald shows that the probes allow for a process termed D-FISH that shows translocations with low false-positive and false-negative results. The probes are detailed in the first paragraph of the Materials and Methods section on page 3358. Results of the assay are shown in figure 1 and Table 1. Dewald concludes on page 3365 that:

> In conclusion, D_FISH is a significant technological advancement in monitoring therapy for CML. D-FISH detects all variant translocations of the Ph chromosome and accurately quantifies disease in CML at diagnosis and at all times during treatment, even for patients in cytogenetic remission.

Dewald et al. does not show a product comprising the two probes used in the method, or probes in a container, or a kit containing the probes.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to collect the probes of Dewald et al. in containers or a kit to facilitate ease of performing the assay shown in Dewald et al. because Dewald et al. shows that the probes are required for a useful clinical diagnostic assay that others in the field of diagnostic assays would have motivation to perform.

Double Patenting

19. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

20. Claims 127-143 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 3 of U.S. Patent No. 6,280,929. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed subject matter of U.S. Patent No. 6,280,929 includes an embodiment of a process that uses two probes that span a breakpoint region. The probes and collections of probes in containers or kits is obvious over a process that uses the same probes.

Conclusion

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie A. Moran can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/John S. Brusca/
Primary Examiner, Art Unit 1631

jsb